Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (Currently Amended) A process for the identification of a microbial gene encoding a gene product that is important to a microbe's ability to infect or sustain an infection in a mammal, which process comprises:

infecting a plurality of mammals with a microbe that has been genetically altered such that the amount of said gene product produced by said genetically altered microbe is regulated by a Tetracycline-Controllable Element (TCE);

where said TCE is a gene regulatory system that controls the expression of the target gene product through its ability to modulate the function of said gene in response to said microbe's exposure to tetracycline, and where said TCE is comprised of a tetracycline-controllable transcription promoter polynucleotide sequence;

where said genetically altered microbe also comprises a polynucleotide sequence encoding a tetracycline resistance protein;

where said polynucleotide sequence encoding a tetracycline resistance protein is contained on a tetracycline resistance and repressor DNA cassette (TRRDC), said TRRDC comprising a tetracycline repressor gene and a tetracycline resistance gene;

where said TCE is operably linked to a polynucleotide sequence encoding a reporter gene (RG) and a target gene (TG);

exposing the plurality of mammals to tetracycline;

once an infection with the genetically altered microbe is established, removing the tetracycline exposure of a portion of the plurality of mammals, such that a first group of the plurality of mammals is exposed to tetracycline and a second group of the plurality of mammals is not exposed to tetracycline; and

comparing the degree of infection, microbe levels, or survival rates of the mammals in the first group and the second group wherein a [mathematically significant] difference between the two groups of animals in the survival rates, levels of microbes, or levels of infection present identifies the gene product as important to a microbe's ability to infect or sustain an infection in a mammal.

2. (Canceled)

3. (Previously Presented) The process of claim 1, where said tetracycline-controllable transcription promoter polynucleotide sequence is a prokaryotic transcription promoter.

4. (Canceled)

5. (Currently Amended) The process of claim [[4]] 1, where said reporter gene encodes a β-lactamase.

6. (Canceled)

7. (Currently Amended) The process of claim [[6]] 1, ~~where said TCE is operably linked to a polynucleotide sequence encoding a reporter gene (RG) and a target gene (TG) and~~ where the TCE, the TRRDC, the RG, and the TG are all on the same DNA cassette, referred to as a Regulatory DNA Cassette (RDC).

8. (Currently Amended) The process of claim [[6]] 1, where said TRRDC promoter is operably linked to the TCE, the tetracycline repressor gene comprises the structural gene *tetM*, and the tetracycline resistance gene comprises the structural gene *tetR*.

9. (Currently Amended) The process of claim 1, where said ~~mathematically significant~~ difference between the two groups of animals is a ~~mathematically significant~~ difference in the levels of microbes or levels of infection present in the mammals.

10. (Currently Amended) The process of claim 1, where said ~~mathematically significant~~ difference between the two groups of animals is a ~~mathematically significant~~ difference in the survival rates of the groups of animals.

11. (Currently Amended) The process of claim 1, where said ~~mathematically significant~~ difference between the two groups of animals shows that animals exposed to tetracycline have poorer health, higher rates of infection, lower survival or higher levels of microbes than animals not exposed to tetracycline.

12. (Currently Amended) The process of claim [[6]] 1, where said tetracycline resistance gene of said TRRDC comprises sequences from the *Staphylococcus aureus tetM* gene.

13. (Currently Amended) The process of claim [[6]] 1, where said tetracycline repressor gene of said TRRDC is obtained from the Tn10 transposon.

14. (Currently Amended) The process of claim [[6]] 1, where said TRRDC comprises the sequence of SEQ ID NO:35 or SEQ ID NO:36.

15. (Previously Presented) The process of claim 1, where said infected mammals are mice.

16. (Previously Presented) The process of claim 1, where said genetically altered microbe is a Staphylococcus species.

17. (Previously Presented) The process of claim 16, where said Staphylococcus species is *Staphylococcus aureus.*

18. (Previously Presented) The process of claim 1, where said microbe is a virus.

19. (Previously Presented) The process of claim 1, where said microbe is a lower eukaryote.

20. (Previously Presented) The process of claim 1, where said microbe is a yeast.

21. (Withdrawn) An isolated DNA molecule for integrating a heterologous polynucleotide sequence at a pre-determined location in a prokaryotic chromosome to operably control an endogenous prokaryotic gene, said DNA molecule comprising recombining element (RE) and a tetracycline controllable element (TCE), said TCE comprising a tetracycline-controllable prokaryotic transcription promoter polynucleotide sequence flanked at its 5' end by said RE, said RE comprising additional polynucleotide sequences of sufficient length for homologous recombination between the isolated DNA molecule and the prokaryotic chromosome.

22. (Withdrawn) The isolated DNA molecule of claim 21 further comprising a polynucleotide sequence encoding a reporter gene operably linked to said TCE.

23. (Withdrawn) The isolated DNA molecule of claim 22 wherein said reporter gene is beta-lactamase.

24. (Withdrawn) The isolated DNA molecule of claim 21 further comprising at least one prokaryotic transcription terminator polynucleotide sequence positioned between the RE and the TCE.

25. (Withdrawn) The isolated DNA molecule of claim 21 further comprising a polynucleotide sequence encoding a prokaryotic tetracycline resistance protein operably linked to a prokaryotic transcription promoter polynucleotide sequence positioned between the RE and the TCE.

26. (Withdrawn) The isolated DNA molecule of claim 25 wherein the tetracycline resistance protein is derived from the *Staphylococcus aureus tetM* gene.

27. (Withdrawn) The isolated DNA molecule of claim 21 further comprising a polynucleotide sequence encoding a prokaryotic tetracycline repressor protein operably linked to a tetracycline-controllable prokaryotic transcription promoter polynucleotide sequence positioned between the RE and the TCE.

28. (Withdrawn) The isolated DNA molecule of claim 27, wherein the tetracycline repressor is a a *tetR* gene derived from the Tn10 transposon.

29. (Withdrawn) A recombinant vector comprising the isolated DNA molecule of claim 21 in a form suitable for transformation of a host cell.

30. (Withdrawn) A host cell comprising the recombinant vector of claim 29.

31. (Withdrawn) A prokaryotic host cell comprising the DNA molecule of claim 21 wherein the DNA molecule is integrated at a pre-determined location in the host cell chromosome.

32. (Withdrawn) The isolated DNA molecule of claim 21, wherein said recombining elements are comprised of polynucleotides selected from Sequence ID NO: 40, 41, 42 and 43.

33. (Withdrawn) The isolated DNA molecule of claim 21, wherein said recombining elements are comprised of polynucleotides selected from Sequence ID NO: 44 and 45.

34. (Withdrawn) The isolated DNA molecule of claim 21, wherein said tetracycline-controllable element is comprised of polynucleotide Sequence ID NO: 37.

35. (Withdrawn) The isolated DNA molecule of claim 21, further comprising a polynucleotide sequence encoding a reporter gene operably linked to said tetracycline-controllable element.

36. (Withdrawn) The isolated DNA molecule of claim 21, wherein said tetracycline-controllable element is comprised of polynucleotide Sequence ID NO: 37.

37. (Withdrawn) The isolated DNA molecule of claim 21, wherein said reporter gene is beta-lactamase.

38. (Withdrawn) The isolated DNA molecule of claim 21, wherein said reporter gene is beta-lactamase, selected from SEQ ID NO: 38 and 39.

39. (Withdrawn) The isolated DNA molecule of claim 21 wherein the tetracycline resistance protein is derived from the *Staphylococcus aureus tetM* gene.

40. (Withdrawn) The isolated DNA molecule of claim 21 wherein the tetracycline resistance protein is derived from the *Staphylococcus aureus tetM* gene selected from SEQ ID NO: 34.

41. (Withdrawn) The isolated DNA molecule of claim 21 wherein the tetracycline repressor is a a *tetR* gene derived from the Tn10 transposon and selected from SEQ ID NO: 35 and 36.

42. (Withdrawn) The isolated DNA molecule of claim 21, further comprising a polynucleotide sequence comprising at least one prokaryotic transcription terminator seqeunce (SEQ ID NO:33) positioned between the tetracycline-controllable element and one recombining element.

43. (Withdrawn) The isolated DNA molecule of claim 21, further comprising a polynucleotide sequence encoding a prokaryotic tetracycline resistance protein operably linked to a transcription promoter polynucleotide sequence.

44. (Withdrawn) The isolated DNA molecule of claim 21, further comprising a polynucleotide sequence encoding a tetracycline repressor protein operably linked to a transcription promoter polynucleotide sequence.

45. (Withdrawn) A recombinant vector comprising the isolated DNA molecule of claim 21 in a form suitable for transformation of a host cell.

46. (Withdrawn) An isolated DNA molecule for integrating a polynucleotide sequence including tetracycline-controllable elements (TCE) at a pre-determined location in a target DNA molecule, said isolated DNA molecule comprising the following DNA elements fused in sequence:

a) a first prokaryotic transcription terminator polynucleotide sequence;

b) a second prokaryotic transcription terminator polynucleotide sequence;

c) a polynucleotide sequence encoding a prokaryotic tetracycline resistance protein;

d) a polynucleotide sequence encoding a prokaryotic repressor protein;

e) a first tetracycline-controllable prokaryotic transcription promoter polynucleotide sequence;

f) a second tetracycline-controllable prokaryotic transcription promoter polynucleotide sequence; and

g) a polynucleotide sequence encoding a reporter protein;

said isolated DNA molecule comprising a polynucleotide sequence including the TCE flanked at the end opposite the polynucleotide sequence encoding said reporter protein by additional polynucleotide sequences of sufficient length for homologous recombination between the isolated DNA molecule and the target DNA molecule at a pre-determined location.

47. (Withdrawn) A recombinant vector comprising the isolated DNA molecule of claim 46 in a form suitable for transformation of a host cell.

48. (Withdrawn) A prokaryotic host cell comprising the DNA molecule of claim 46 wherein the DNA molecule is integrated at a pre-determined location in the host cell chromosome.

49. (Withdrawn) The isolated DNA molecule of claim 46, wherein said recombining elements are comprised of polynucleotides selected from Sequence ID NO: 40, 41, 42 and 43.

50. (Withdrawn) The isolated DNA molecule of claim 46, wherein said recombining elements are comprised of polynucleotides selected from Sequence ID NO: 44 and 45.

51. (Withdrawn) The isolated DNA molecule of claim 46, wherein said tetracycline-controllable element is comprised of polynucleotide Sequence ID NO: 37.

52. (Withdrawn) The isolated DNA molecule of claim 46, further comprising a polynucleotide sequence encoding a reporter gene operably linked to said tetracycline-controllable element.

53. (Withdrawn) The isolated DNA molecule of claim 46, wherein said tetracycline-controllable element is comprised of polynucleotide Sequence ID NO: 37.

54. (Withdrawn) The isolated DNA molecule of claim 46, wherein said reporter gene is beta-lactamase.

55. (Withdrawn) The isolated DNA molecule of claim 46, wherein said reporter gene is beta-lactamase, selected from SEQ ID NO: 38 and 39.

56. (Withdrawn) The isolated DNA molecule of claim 46, wherein the tetracycline repressor protein is derived from the *Staphylococcus aureus tetM* gene.

57. (Withdrawn) The isolated DNA molecule of claim 46, wherein the tetracycline repressor protein is derived from the *Staphylococcus aureus tetM* gene selected from SEQ ID NO: 34.

58. (Withdrawn) The isolated DNA molecule of claim 46, wherein the tetracycline repressor is a *tetR* gene derived from the Tn10 transposon and selected from SEQ ID NO: 35 and 36.

59. (Withdrawn) An isolated DNA molecule comprising a tetracycline-controllable transcription promoter polynucleotide sequence operably linked to a microbial gene.

60. (Withdrawn) The isolated DNA molecule of claim 59, wherein said tetracycline-controllable element is comprised of polynucleotide Sequence ID NO: 37.

61. (Withdrawn) The isolated DNA molecule of claim 60, further comprising a polynucleotide sequence encoding a reporter gene operably linked to said tetracycline-controllable element.

62. (Withdrawn) The isolated DNA molecule of claim 61, wherein said reporter gene is beta-lactamase.

63. (Withdrawn) The isolated DNA molecule of claim 62, wherein said reporter gene is beta-lactamase selected from SEQ ID NO: 38 and 39.

64. (Withdrawn) The isolated DNA molecule of claim 59, further comprising a polynucleotide sequence encoding a a tetracycline resistance (or protection) and repressor DNA cassette (TRRDC) operably linked to a transcription promoter polynucleotide sequence.

65. (Withdrawn) The isolated DNA molecule of claim 64, further comprising a polynucleotide sequence encoding a prokaryotic a tetracycline resistance (or protection) and repressor DNA cassette (TRRDC), operably linked to a transcription promoter polynucleotide sequence.

66. (Withdrawn) The isolated DNA molecule of claim 65, wherein said tetracycline resistance (or protection) and repressor DNA cassette (TRRDC) is derived from a *Staphylococcus aureus tetM* gene.

67. (Withdrawn) The isolated DNA molecule of claim 66, wherein said tetracycline resistance (or protection) and repressor DNA cassette (TRRDC) is derived from the *Staphylococcus aureus tetM* gene comprised of SEQ ID NO: 34.

68. (Withdrawn) The isolated DNA molecule of claim 67, wherein said tetracycline resistance (or protection) and repressor DNA cassette (TRRDC) is a TN10 derived tetracycline repressor.

69. (Withdrawn) The isolated DNA molecule of claim 68, wherein the a tetracycline resistance (or protection) and repressor DNA cassette (TRRDC) is a TN10 derived tetracycline repressor selected from the polynucleotides of SEQ ID NO: 35 and 36.

70. (Withdrawn) A recombinant vector comprising the isolated DNA molecule of claim 21 in a form suitable for transformation of a host cell.

71. (Withdrawn) A host cell comprising the recombinant vector of claim 70.

72. (Withdrawn) A recombinant vector comprising the isolated DNA molecule of claim 46 in a form suitable for transformation of a host cell.

73. (Withdrawn) A host cell comprising the recombinant vector of claim 72

74. (Withdrawn) A recombinant vector comprising the isolated DNA molecule of claim 59 in a form suitable for transformation of a host cell.

75. (Withdrawn) A host cell comprising the recombinant vector of claim 74.

76. (Withdrawn) A process to regulate expression of an endogenous prokaryotic gene comprising the cultivation of the prokaryotic cell in medium with a controlled amount of tetracycline or a tetracycline analog.

77. (Currently Amended) A process to regulate expression of a gene product by a microbe in a mammalian host with tetracycline or a tetracycline analog, said process comprising:

infecting a mammalian host with a microbe that has been genetically altered such that the amount of said gene product produced by said genetically altered microbe is regulated by a Tetracycline-Controllable Element (TCE);

where said TCE is a gene regulatory system that controls the expression of the target gene product through its ability to modulate the function of said gene in response to said microbe's exposure to tetracycline, and where said TCE is comprised of a tetracycline-controllable transcription promoter polynucleotide sequence;

where said genetically altered microbe also comprises a polynucleotide sequence encoding a tetracycline resistance protein;

where said polynucleotide sequence encoding a tetracycline resistance protein is contained on a tetracycline resistance and repressor DNA cassette (TRRDC), said TRRDC comprising a tetracycline repressor gene and a tetracycline resistance gene;

where said TCE is operably linked to a polynucleotide sequence encoding a reporter gene (RG) and a target gene (TG); and

exposing the mammalian host to tetracycline.

78. (Previously Presented) The process of claim 77, further comprising, once an infection with the genetically altered microbe is established, removing the tetracycline exposure of the mammalian host.

79. (Previously Presented) The process of claim 1, where said plurality of mammals are exposed to tetracycline while being infected with the genetically altered microbe.

80. (Previously Presented) The process of claim 1, where said plurality of mammals are exposed to tetracycline by adding tetracycline to the drinking water.

81. (Canceled)

82. (New) The process of claim 77, where the TCE, the TRRDC, the RG, and the TG are all on the same DNA cassette, referred to as a Regulatory DNA Cassette (RDC).